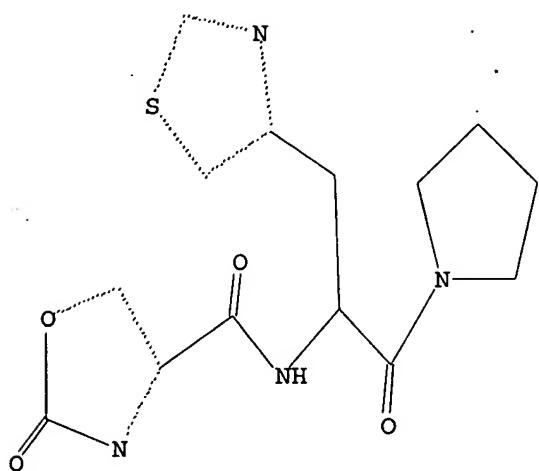


## EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	1010	(548/204).CCLS.	US-PGPU B; USPAT; USOCR; EPO; JPO; DERWEN T; IBM_TDB	OR	OFF	2006/12/10 11:41
L2	19210	AMINO ALCOHOL	US-PGPU B; USPAT; USOCR; EPO; JPO; DERWEN T; IBM_TDB	ADJ	ON	2006/12/10 11:42
L3	35	L1 AND L2	US-PGPU B; USPAT; USOCR; EPO; JPO; DERWEN T; IBM_TDB	ADJ	ON	2006/12/10 11:42
L4	19	L3 AND PEPTIDE	US-PGPU B; USPAT; USOCR; EPO; JPO; DERWEN T; IBM_TDB	ADJ	ON	2006/12/10 11:42

10/723/36

10/723/36



Structure attributes must be viewed using STN Express query preparation.

=> S L1

SAMPLE SEARCH INITIATED 10:31:49 FILE 'REGISTRY'  
SAMPLE SCREEN SEARCH COMPLETED - 3 TO ITERATE

100.0% PROCESSED 3 ITERATIONS 2 ANSWERS  
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 3 TO 163

PROJECTED ANSWERS: 2 TO 124

L2 2 SEA SSS SAM L1

=> S L1 FULL

FULL SEARCH INITIATED 10:31:56 FILE 'REGISTRY'  
FULL SCREEN SEARCH COMPLETED - 72 TO ITERATE

100.0% PROCESSED 72 ITERATIONS 41 ANSWERS  
SEARCH TIME: 00.00.01

L3 41 SEA SSS FUL L1

=> FILE CAPLUS

COST IN U.S. DOLLARS

SINCE FILE

ENTRY

TOTAL

FULL ESTIMATED COST

SESSION

166.94

167.57

FILE 'CAPLUS' ENTERED AT 10:32:02 ON 10 DEC 2006

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10/723/36

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FILE COVERS 1907 - 10 Dec 2006 VOL 145 ISS 25  
FILE LAST UPDATED: 8 Dec 2006 (20061208/ED)

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L4 6 L3

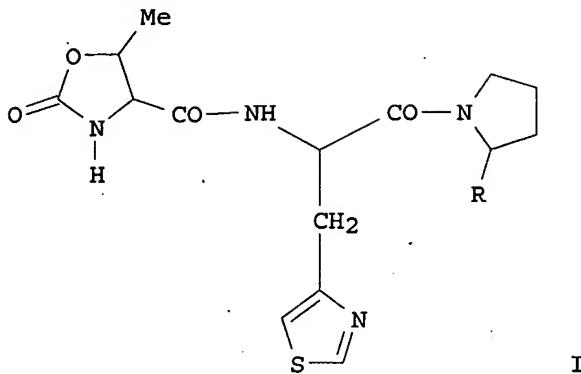
=> D IBIB ABS HITSTR TOT

L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 2006:234805 CAPLUS  
DOCUMENT NUMBER: 144:299445  
TITLE: A pharmaceutical composition for treating ataxia, multiple system atrophy or balance disorders  
INVENTOR(S): Yoshikawa, Takayoshi; Katsuura, Goro  
PATENT ASSIGNEE(S): Shionogi & Co., Ltd., Japan  
SOURCE: PCT Int. Appl., 22 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006028277	A1	20060316	WO 2005-JP16994	20050908
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRIORITY APPLN. INFO.:			JP 2004-261977	A 20040909
			US 2004-613717P	P 20040929

GI

10/22/88



AB This invention provides a pharmaceutical composition for treating spinocerebellar ataxia (or atrophy, degeneration) or multiple system atrophy, or for improving ataxia or equilibrium disturbance comprising a compound

of the formula I (R = Me, cyano, carbamoyl), a pharmaceutically acceptable salt, or a solvate thereof as an active ingredient. For example, I trihydrate (R = Me) was prepared (yield 80.3%) and its effect on ataxia of Rolling Mouse Nagoya was investigated. An improvement of ataxia of oral I trihydrate (R = Me) at 1 mg/kg and 3 mg/kg was demonstrated, being  $\geq 30$  and  $\geq 100$  times more effective than control compds., resp. A capsule formulation containing compound I 10 mg, lactose 90 mg, corn starch 42 mg, and hydroxypropyl cellulose 3 mg was provided.

IT 204385-91-1 204386-74-3

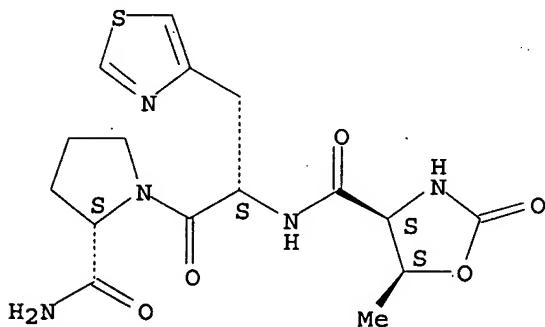
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(composition containing oxooxazolidinylcarbonyl thiazolylalanyl pyrrolidine derivative for treating ataxia, multiple system atrophy or balance disorders)

RN 204385-91-1 CAPPLUS

CN L-Prolinamide, (4S,5S)-5-methyl-2-oxo-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

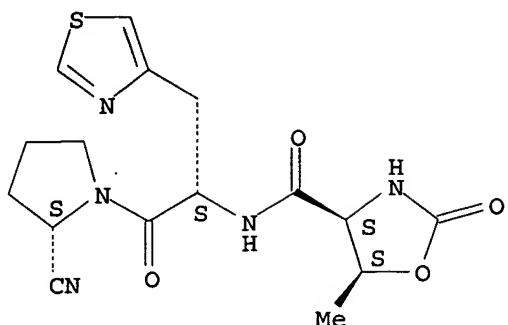


RN 204386-74-3 CAPPLUS

CN 4-Oxazolidinecarboxamide, N-[(1S)-2-[(2S)-2-cyano-1-pyrrolidinyl]-2-oxo-1-(4-thiazolylmethyl)ethyl]-5-methyl-2-oxo-, (4S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

~~10/22/819~~



IT 879122-88-0

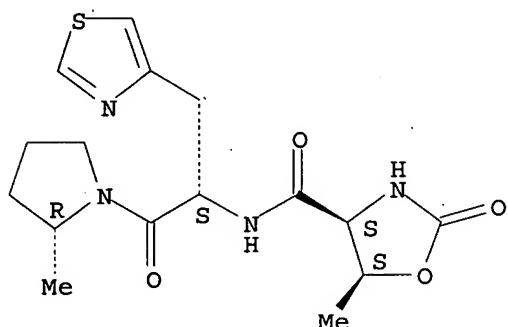
RL: RCT (Reactant); RACT (Reactant or reagent)

(composition containing oxooxazolidinylcarbonyl thiazolylalanyl pyrrolidine derivative for treating ataxia, multiple system atrophy or balance disorders)

RN 879122-88-0 CAPLUS

CN 4-Oxazolidinecarboxamide, 5-methyl-N-[(1S)-2-[(2R)-2-methyl-1-pyrrolidinyl]-2-oxo-1-(4-thiazolylmethyl)ethyl]-2-oxo-, monohydrate, (4S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● H<sub>2</sub>O

IT 204386-76-5P 879122-87-9P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

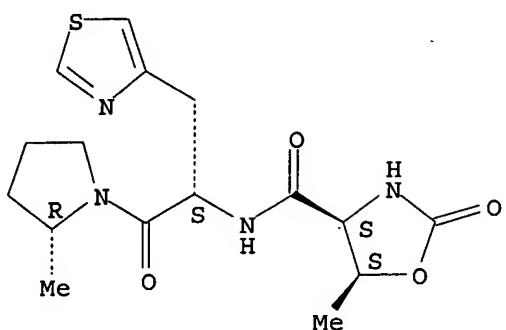
(composition containing oxooxazolidinylcarbonyl thiazolylalanyl pyrrolidine derivative for treating ataxia, multiple system atrophy or balance disorders)

RN 204386-76-5 CAPLUS

CN 4-Oxazolidinecarboxamide, 5-methyl-N-[(1S)-2-[(2R)-2-methyl-1-pyrrolidinyl]-2-oxo-1-(4-thiazolylmethyl)ethyl]-2-oxo-, (4S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

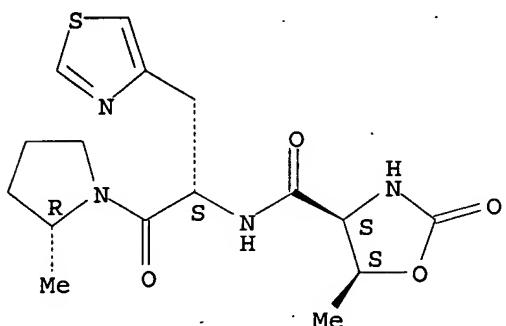
10/22/019



RN 879122-87-9 CAPLUS

CN 4-Oxazolidinecarboxamide, 5-methyl-N-[(1S)-2-[(2R)-2-methyl-1-pyrrolidinyl]-2-oxo-1-(4-thiazolylmethyl)ethyl]-2-oxo-, trihydrate, (4S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● 3 H<sub>2</sub>O

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN ,

ACCESSION NUMBER: 2002:171718 CAPLUS

DOCUMENT NUMBER: 136:232293

TITLE: Preparation process of chiral N-(2-(4-thiazolyl)-1-(2-methylpyrrolidinylcarbonyl)ethyl)-4-methyl-2-oxo-oxazolidine-5-carbamide as antiparkinsonian agent

INVENTOR(S): Shinohara, Shunji; Koike, Katsumi

PATENT ASSIGNEE(S): Shionogi & Co., Ltd., Japan

SOURCE: PCT Int. Appl., 52 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002017954	A1	20020307	WO 2001-JP7410	20010829
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,				

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS,  
 LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT,  
 RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,  
 UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
 BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2001082527 A5 20020313 AU 2001-82527 20010829

CA 2420537 AA 20030225 CA 2001-2420537 20010829

EP 1321151 A1 20030625 EP 2001-961157 20010829

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

US 2003191120 A1 20031009 US 2003-362922 20030227

US 7129256 B2 20061031

PRIORITY APPLN. INFO.: JP 2000-262618 A 20000831  
 WO 2001-JP7410 W 20010829

OTHER SOURCE(S): CASREACT 136:232293; MARPAT 136:232293

GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Title compds. [I; A = thiazolyl, imidazolyl; X = single bond, O, S; Y = alkyl, CONR1R2; Z = Q; m = 0, 1, 2, 3, 4; R1, R2 independently = H, alkyl; R3 = H, alkyl; R4 = H, alkyl; R5 = alkyl, H; W = (CH2)n; n = 0, 1, 2, 3] prodrugs, pharmaceutically acceptable salts, solvates, and prodrugs of title compds. are prepared and are found to be useful as therapeutic or preventive agents for Parkinson disease. Thus, the title compound II was prepared from N-tert-butoxycarbonyl-L-(4-thiazolyl)alanine, diphenyldiazomethane, and (4S-cis)-5-methyl-2-oxo-4-oxazolidinecarboxylic acid in five steps.

IT 204386-76-5P

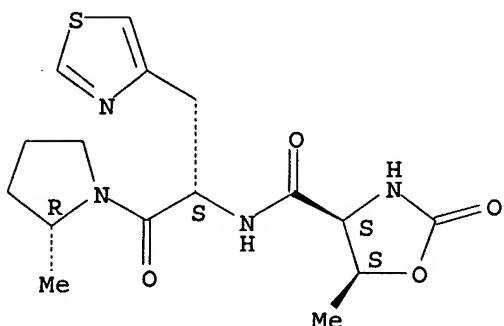
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation process of chiral N-(2-(4-thiazolyl)-1-(2-methylpyrrolidinylcarbonyl)ethyl)-4-methyl-2-oxo-oxazolidine-5-carbamide as antiparkinsonian agent)

RN 204386-76-5 CAPLUS

CN 4-Oxazolidinecarboxamide, 5-methyl-N-[(1S)-2-[(2R)-2-methyl-1-pyrrolidinyl]-2-oxo-1-(4-thiazolylmethyl)ethyl]-2-oxo-, (4S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

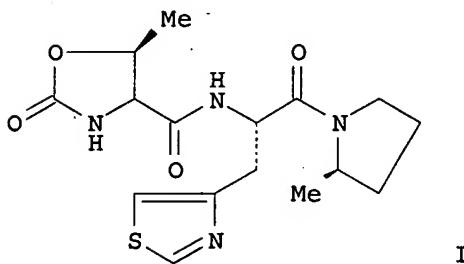


## RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2002:51292 CAPLUS  
 DOCUMENT NUMBER: 136:123639  
 TITLE: Enteric compositions containing physiologically active peptides  
 INVENTOR(S): Sugita, Katsuji; Yoshikawa, Takayoshi  
 PATENT ASSIGNEE(S): Shionogi & Co., Ltd., Japan  
 SOURCE: PCT Int. Appl., 17 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002004016	A1	20020117	WO 2001-JP5543	20010628
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001066347	A5	20020121	AU 2001-66347	20010628
EP 1300155	A1	20030409	EP 2001-943852	20010628
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003175350	A1	20030918	US 2003-332490	20030109
PRIORITY APPLN. INFO.:			JP 2000-209923	A 20000711
			WO 2001-JP5543	W 20010628

OTHER SOURCE(S): MARPAT 136:123639  
 GI



AB Disclosed are enteric compns. for oral administration excellent in absorbability, containing TSH-releasing hormone (TRH) or derivs. thereof as the medicinally active ingredient. A coated enteric tablet was prepared from a TRH derivative I 30, corn starch 17.4, hydroxypropyl cellulose SL 0.7, partially alaphatized starch 1.4, magnesium stearate 0.5, hydroxypropyl Me cellulose (HPMC2910E) 0.8, hydroxypropyl Me cellulose acetate succinate (HPMCAS-LF) 6, tri-Et citrate 0.7, and talc 1.3 mg.

IT 389119-11-3  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

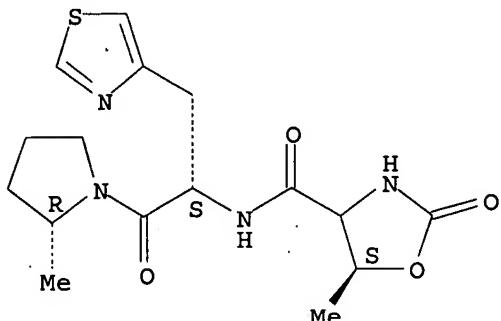
~~10/27/01~~

(enteric compns. containing TRH derivs. and enteric materials)

RN 389119-11-3 CAPLUS

CN 4-Oxazolidinecarboxamide, 5-methyl-N-[(1S)-2-[(2R)-2-methyl-1-pyrrolidinyl]-2-oxo-1-(4-thiazolylmethyl)ethyl]-2-oxo-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:690970 CAPLUS

DOCUMENT NUMBER: 131:314180

TITLE: Oral preparations containing TRH derivatives

INVENTOR(S): Sugita, Katsuji; Satoh, Norihito; Yoshikawa, Takanori

PATENT ASSIGNEE(S): Shionogi & Co., Ltd., Japan

SOURCE: PCT Int. Appl., 20 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9953941	A1	19991028	WO 1999-JP2006	19990415
W: JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				

PRIORITY APPLN. INFO.: JP 1998-104993 A 19980415

AB Preps. for the oral administration of TRH derivs. characterized by containing the TRH derivs., medium-chain triglycerides and, if desired, lecithin. Use of these preps. makes it possible to improve the oral absorbability of the TRH derivs. thereby elevating the bioavailability thereof.

IT 204385-91-1 204386-74-3 204386-76-5

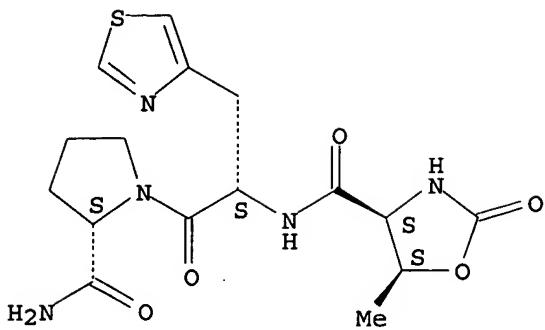
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (oral preps. containing TRH derivs.)

RN 204385-91-1 CAPLUS

CN L-Prolinamide, (4S,5S)-5-methyl-2-oxo-4-oxazolidinecarboxyl-3-(4-thiazolyl)-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

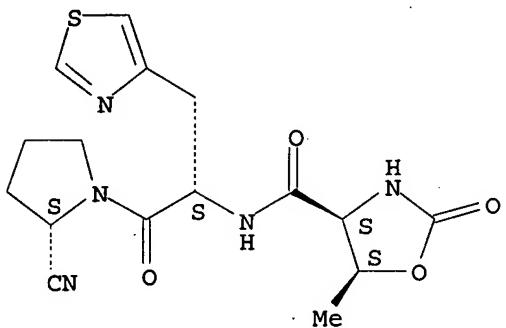
10/229,819



RN 204386-74-3 CAPLUS

CN 4-Oxazolidinecarboxamide, N-[(1S)-2-[(2S)-2-cyano-1-pyrrolidinyl]-2-oxo-1-(4-thiazolylmethyl)ethyl]-5-methyl-2-oxo-, (4S,5S)- (9CI) (CA INDEX NAME)

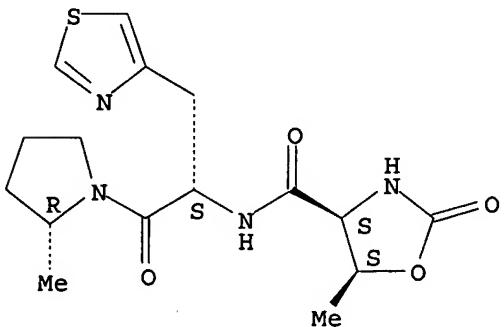
Absolute stereochemistry. Rotation (-).



RN 204386-76-5 CAPLUS

CN 4-Oxazolidinecarboxamide, 5-methyl-N-[(1S)-2-[(2R)-2-methyl-1-pyrrolidinyl]-2-oxo-1-(4-thiazolylmethyl)ethyl]-2-oxo-, (4S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:576919 CAPLUS

DOCUMENT NUMBER: 131:200096

TITLE: Process for producing 4-thiazolylmethyl halide,

10/229,819

INVENTOR(S) :  $\beta$ -(4-thiazolyl)alanine, and peptide  
Uenaka, Masaaki; Nagai, Masahiko; Kobayashi, Naotake  
PATENT ASSIGNEE(S) : Shionogi & Co., Ltd., Japan  
SOURCE : PCT Int. Appl., 33 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9945000	A1	19990910	WO 1999-JP975	19990301
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9926423	A1	19990920	AU 1999-26423	19990301
EP 1069118	A1	20010117	EP 1999-906538	19990301
EP 1069118	B1	20040922		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
TW 530052	B	20030501	TW 1999-88103061	19990301
AT 277024	E	20041015	AT 1999-906538	19990301
ES 2229680	T3	20050416	ES 1999-906538	19990301
JP 3811885	B2	20060823	JP 2000-534543	19990301
US 6506903	B1	20030114	US 2000-622441	20000817
PRIORITY APPLN. INFO.:			JP 1998-49259	A 19980302
			WO 1999-JP975	W 19990301
OTHER SOURCE(S) :	CASREACT 131:200096; MARPAT 131:200096			
GI				

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The process for producing a compound represented by general formula (I) (wherein R1 is hydrogen or halogeno and X is halogeno) comprises reacting 4-methylthiazole with an N-halosuccinimide in a solvent in the presence of a radical initiator. A process for producing a 4-thiazolylalanine derivative (II and III; R2' is an amino acid-protecting group) comprises coupling of 4-thiazolylmethyl halide (I) with aminomalonate of formula R2NHCH(CO2R3)2 (R2 is an amino acid protective-group; R3 is lower alkyl) to give amino(4-thiazolylmethyl)malonate [I; X = C(CO2R3)2NHR2], followed by hydrolysis, decarboxylation, and optical resolution. Moreover, the 4-thiazolylalanine derivative undergoes peptide bond formation to give dipeptide amides [IV; Y is (un)substituted alkyl]. Thus, 163.5 g 4-methylthiazole was dissolved in 3 L chlorobenzene, heated to 130°, treated with 242 g N-chlorosuccinimide and 13.5 g 2,2'-azobisisbutyronitrile, and kept at 160° for 15 min to give, after workup and treatment with 4 N HCl/EtOAc, 43.5% 4-chloromethylthiazole hydrochloride (V.HCl). V.HCl (154 g) was dissolved in 0.5 L H2O and treated with 3 L toluene and 113 g NaHCO3, followed by washing the organic layer and extracting the aqueous layer, drying the combined organic layer over MgSO4, and distilling off the solvent, to give 98% V. To 20% NaOMe/MeOH (306 g) was added 96 g di-Et acetamidomalonate, refluxed for 2

h, treated with a solution of 124 g V containing 10% PhMe in ethanol (0.6 L) at 50°, and stirred at 50° for 3 h to give 72.5% I [X = C(CO<sub>2</sub>Et)<sub>2</sub>NHAc]. The latter diester (201.2 g) was dissolved in 3 N aqueous NaOH (960 mL), stirred at 50° for 1.5 h, treated with 100 mL concentrated HCl to adjust pH = 3.5, stirred at 100° for 3 h, cooled, treated with 120 g immobilized acylase, followed by adjusting pH = 6.7, stirred at 37° for 4 h, and filtered. To the filtrate were added 500 mL dioxane, 90.8 g di-tert-Bu dicarbonate, and 58 mL Et<sub>3</sub>N, stirred at 25° for 2 h, and extracted with 1 L EtOAc to give 40% III (R<sub>2'</sub> = Boc). The latter N-tert-butoxycarbonyl-(4-thiazolyl)alanine was converted into a dipeptide (VI) in 4 steps.

IT 204386-76-5P

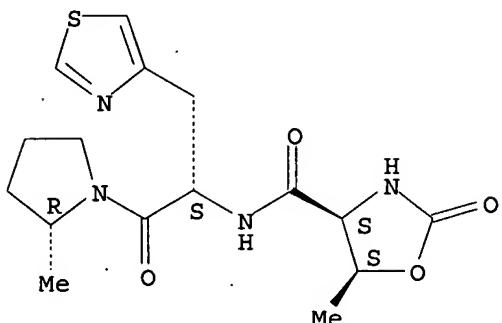
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of thiazolylmethyl halide by halogenation of methylthiazole, its coupling with aminomalonate to amino(thiazolylmethyl)malonate, and conversion to  $\beta$ -(4-thiazolyl)alanine and peptide)

RN 204386-76-5 CAPLUS

CN 4-Oxazolidinecarboxamide, 5-methyl-N-[(1S)-2-[(2R)-2-methyl-1-pyrrolidinyl]-2-oxo-1-(4-thiazolylmethyl)ethyl]-2-oxo-, (4S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:163612 CAPLUS

DOCUMENT NUMBER: 128:230695

TITLE: Preparation of novel peptide derivatives having thiazolyl-alanine residue

INVENTOR(S): Sugawara, Tamio; Yoshikawa, Takayoshi; Tada, Yukio

PATENT ASSIGNEE(S): Shionogi & Co., Ltd., Japan

SOURCE: PCT Int. Appl., 139 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9808867	A1	19980305	WO 1997-JP2917	19970822
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ,				

VN, YU, ZW  
 RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,  
 GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,  
 GN, ML, MR, NE, SN, TD, TG  
 CA 2264268 AA 19980305 CA 1997-2264268 19970822  
 CA 2264268 C 20031111  
 AU 9738680 A1 19980319 AU 1997-38680 19970822  
 AU 713133 B2 19991125  
 EP 933379 A1 19990804 EP 1997-935856 19970822  
 EP 933379 B1 20060322  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO  
 BR 9712081 A 19990824 BR 1997-12081 19970822  
 CN 1235610 A 19991117 CN 1997-199248 19970822  
 JP 3234236 B2 20011204 JP 1998-511459 19970822  
 AT 321067 E 20060415 AT 1997-935856 19970822  
 PT 933379 T 20060731 PT 1997-935856 19970822  
 ES 2259805 T3 20061016 ES 1997-935856 19970822  
 TW 492977 B 20020701 TW 1997-86112314 19970827  
 MX 9901831 A 20000331 MX 1999-1831 19990224  
 KR 2000035930 A 20000626 KR 1999-701667 19990227  
 US 6319902 B1 20011120 US 1999-230821 19990512  
 PRIORITY APPLN. INFO.: JP 1996-226386 A 19960828  
 JP 1997-90529 A 19970409  
 WO 1997-JP2917 W 19970822

OTHER SOURCE(S) : MARPAT 128:230695  
 GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Peptide derivs. represented by general formula [I; A = 4- or 5-thiazolyl;  
 Y = single bond, O, S; m = 0-4; Y = (un)substituted alkyl or CO<sub>2</sub>H, cyano,  
 CONR<sub>1</sub>R<sub>2</sub>; wherein R<sub>1</sub>, R<sub>2</sub> = H or (un)substituted alkyl or NR<sub>1</sub>R<sub>2</sub> =  
 (un)substituted nonarom. heterocyclyl optionally containing O, N, or S; Z = Q,  
 Q<sub>1</sub>; R<sub>3</sub> = H, (un)substituted alkyl, CO<sub>2</sub>H, or acyl; R<sub>4</sub>, R<sub>5</sub> = H,  
 (un)substituted alkyl; W = (CH<sub>2</sub>)<sub>n</sub>, O, S, (un)substituted NH; wherein n =  
 0, 1, 2, or 3] or pharmacol. acceptable salts or hydrates thereof are  
 prepared. These peptide compds. have improved central nerve activating  
 effects such as sustained acetylcholine-releasing effect, antireserpine  
 effect and spontaneous motility increasing effect as compared with the  
 publicly known TSH releasing hormone TSH-releasing hormone  
 (TRH) (H-pGlu-His-Pro-NH<sub>2</sub>) and TRH derivs. Thus, L-pyroglutamic acid was  
 condensed with 3-(4-thiazolyl)-L-alanyl-L-prolinamide hydrochloride using  
 DCC and N-hydroxysuccinimide in DMF to give the title compound (II; R = Q<sub>2</sub>).  
 II (R = Q<sub>3</sub>) at 24 μmol/kg p.o. increased ≤260% release of  
 acetylcholine from brain in rat 350 h after administration of the compound

IT 204385-84-2P 204385-91-1P 204385-98-8P  
 204386-01-6P 204386-03-8P 204386-25-4P  
 204386-28-7P 204386-30-1P 204386-35-6P  
 204386-37-8P 204386-39-0P 204386-41-4P  
 204386-45-8P 204386-47-0P 204386-50-5P  
 204386-52-7P 204386-54-9P 204386-58-3P  
 204386-60-7P 204386-61-8P 204386-62-9P  
 204386-63-0P 204386-64-1P 204386-66-3P  
 204386-67-4P 204386-68-5P 204386-70-9P  
 204386-71-0P 204386-72-1P 204386-73-2P  
 204386-74-3P 204386-75-4P 204386-76-5P  
 204386-77-6P 204506-84-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological

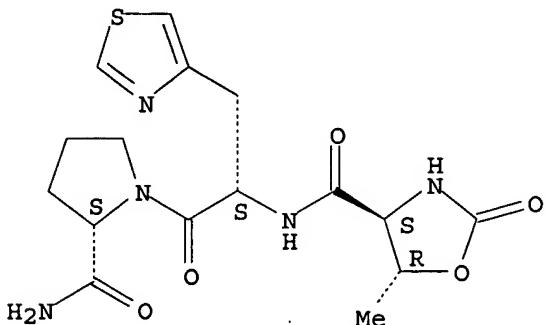
10/229, 819

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of novel peptide derivs. having thiazolylalanine residue as central nerve activators)

RN 204385-84-2 CAPLUS

CN L-Prolinamide, (4S,5R)-5-methyl-2-oxo-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl- (9CI) (CA INDEX NAME)

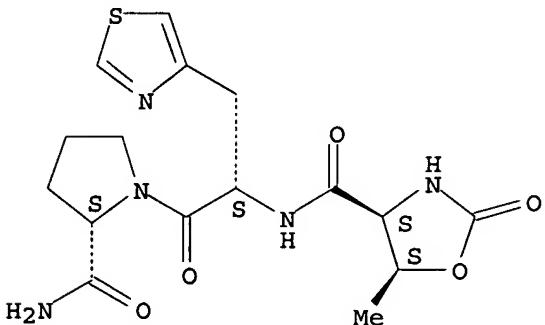
Absolute stereochemistry. Rotation (-).



RN 204385-91-1 CAPLUS

CN L-Prolinamide, (4S,5S)-5-methyl-2-oxo-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl- (9CI) (CA INDEX NAME)

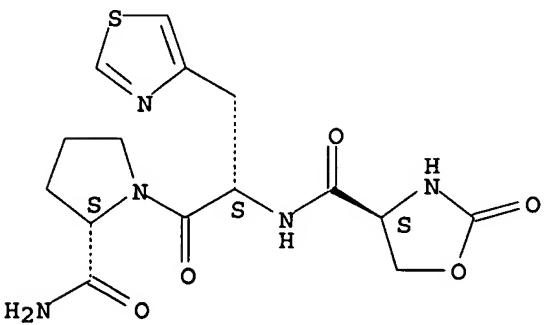
Absolute stereochemistry. Rotation (-).



RN 204385-98-8 CAPLUS

CN L-Prolinamide, (4S)-2-oxo-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

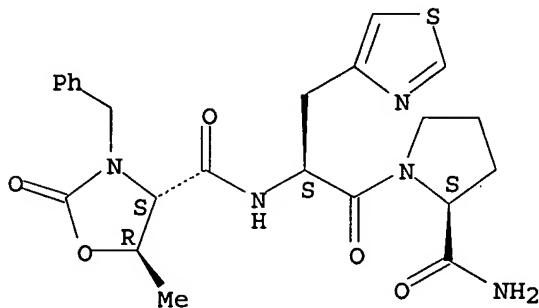


10/229,819

RN 204386-01-6 CAPLUS

CN L-Prolinamide, (4S,5R)-5-methyl-2-oxo-3-(phenylmethyl)-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl- (9CI) (CA INDEX NAME)

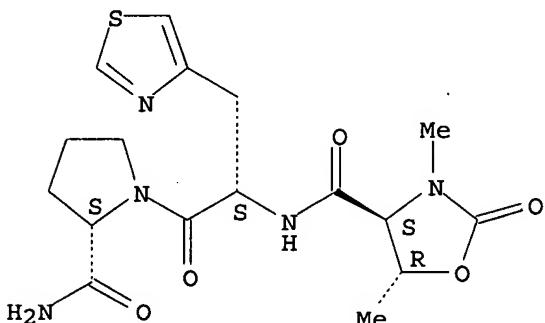
Absolute stereochemistry. Rotation (-).



RN 204386-03-8 CAPLUS

CN L-Prolinamide, (4S,5R)-3,5-dimethyl-2-oxo-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl- (9CI) (CA INDEX NAME)

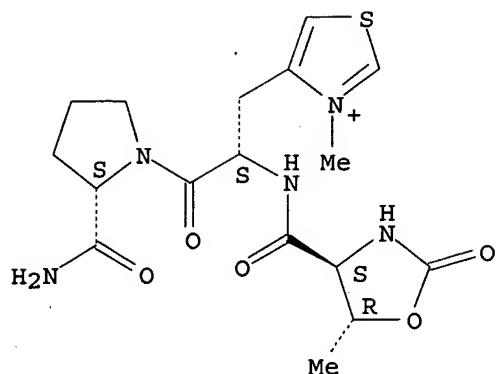
Absolute stereochemistry. Rotation (-).



RN 204386-25-4 CAPLUS

CN L-Prolinamide, (4S,5R)-5-methyl-2-oxo-4-oxazolidinecarbonyl-3-(3-methylthiazolium-4-yl)-L-alanyl-, iodide (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

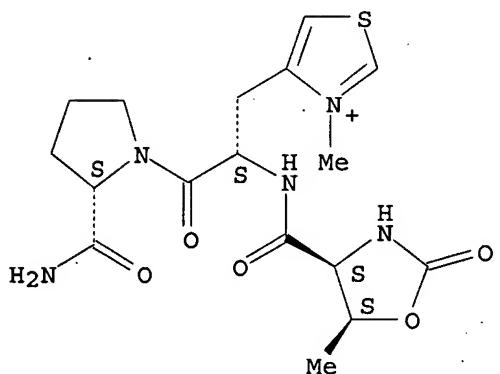


● I -

RN 204386-28-7 CAPLUS

CN L-Prolinamide, (4S,5S)-5-methyl-2-oxo-4-oxazolidinecarbonyl-3-(3-methylthiazolium-4-yl)-L-alanyl-, iodide (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

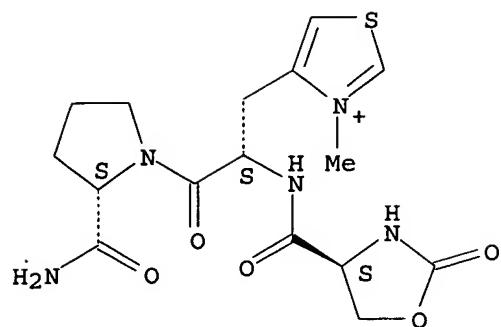


● I -

RN 204386-30-1 CAPLUS

CN L-Prolinamide, (4S)-2-oxo-4-oxazolidinecarbonyl-3-(3-methylthiazolium-4-yl)-L-alanyl-, iodide (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

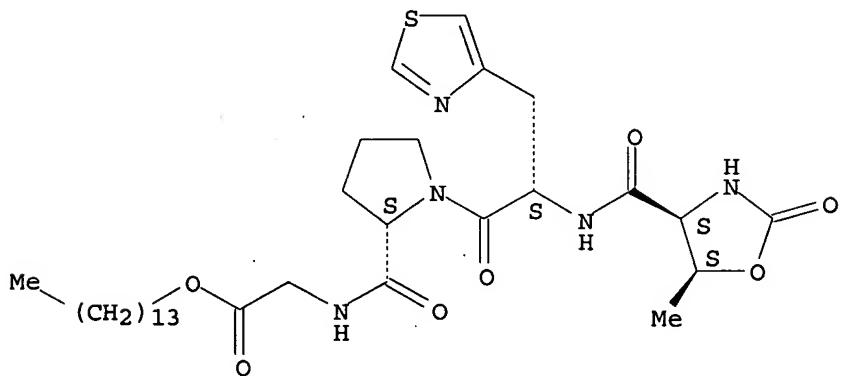


● I -

RN 204386-35-6 CAPLUS

CN Glycine, (4S,5S)-5-methyl-2-oxo-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl-L-prolyl-, tetradecyl ester (9CI) (CA INDEX NAME)

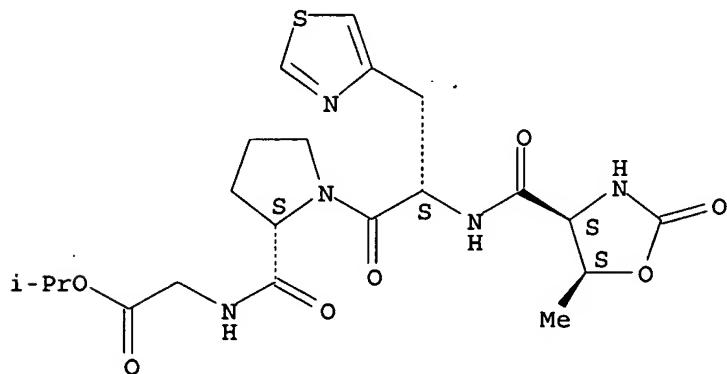
Absolute stereochemistry. Rotation (-).



RN 204386-37-8 CAPLUS

CN Glycine, (4S,5S)-5-methyl-2-oxo-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl-L-prolyl-, 1-methylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



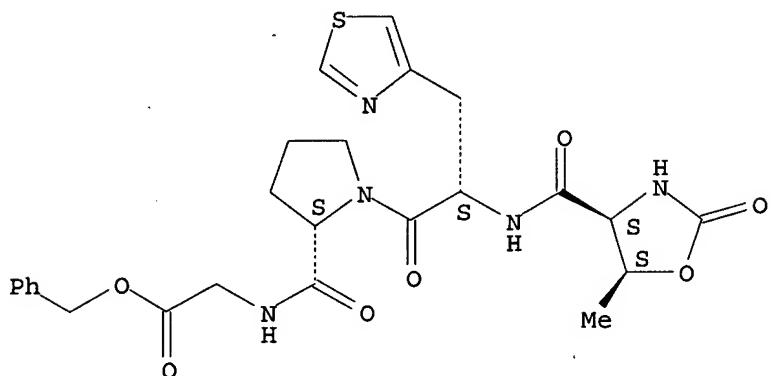
RN 204386-39-0 CAPLUS

CN Glycine, (4S,5S)-5-methyl-2-oxo-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-

10/229,819

alanyl-L-prolyl-, phenylmethyl ester (9CI) (CA INDEX NAME)

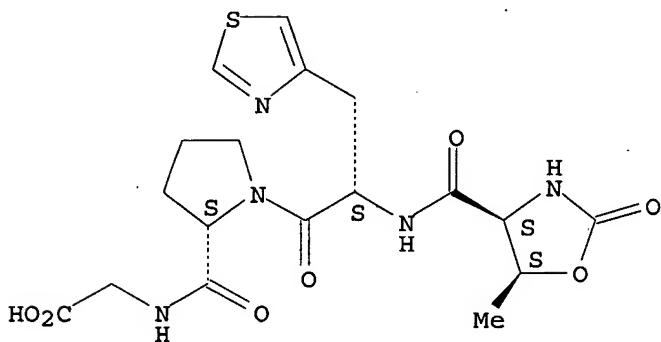
Absolute stereochemistry. Rotation (-).



RN 204386-41-4 CAPLUS

CN Glycine, (4S,5S)-5-methyl-2-oxo-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl-L-prolyl- (9CI) (CA INDEX NAME)

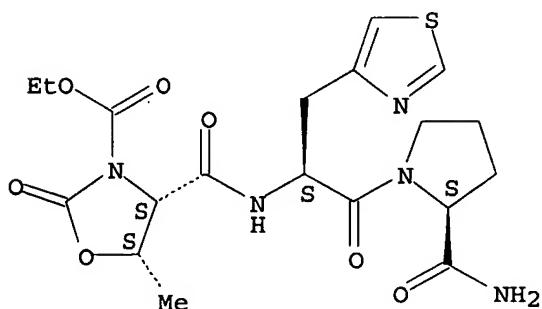
Absolute stereochemistry. Rotation (-).



RN 204386-45-8 CAPLUS

CN L-Prolinamide, (4S,5S)-3-(ethoxycarbonyl)-5-methyl-2-oxo-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

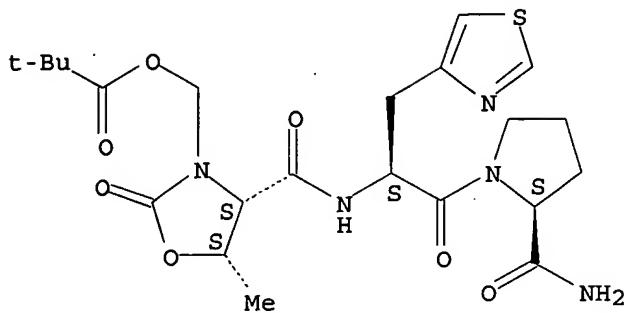


RN 204386-47-0 CAPLUS

CN L-Prolinamide, (4S,5S)-3-[(2,2-dimethyl-1-oxopropoxy)methyl]-5-methyl-2-oxo-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl- (9CI) (CA INDEX NAME)

10/229,819

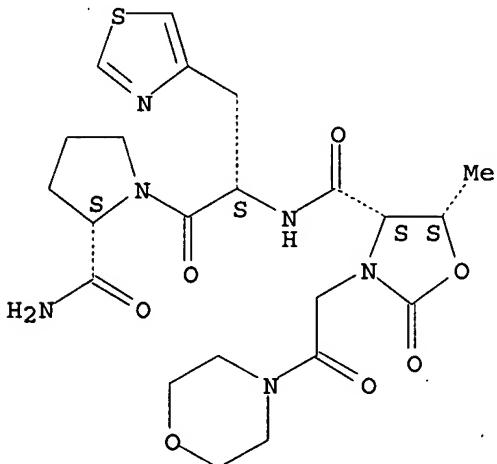
Absolute stereochemistry. Rotation (-).



RN 204386-50-5 CAPLUS

CN L-Prolinamide, (4S,5S)-5-methyl-3-[2-(4-morpholinyl)-2-oxoethyl]-2-oxo-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl- (9CI) (CA INDEX NAME)

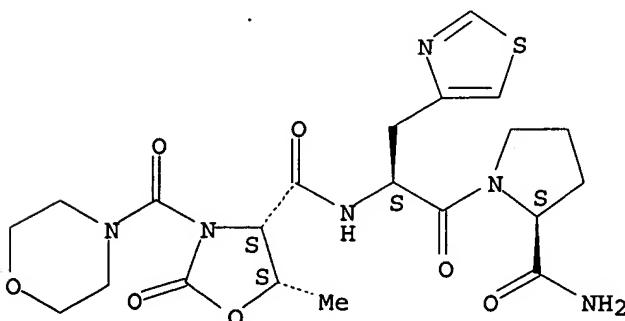
Absolute stereochemistry. Rotation (-).



RN 204386-52-7 CAPLUS

CN L-Prolinamide, (4S,5S)-5-methyl-3-(4-morpholinylcarbonyl)-2-oxo-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



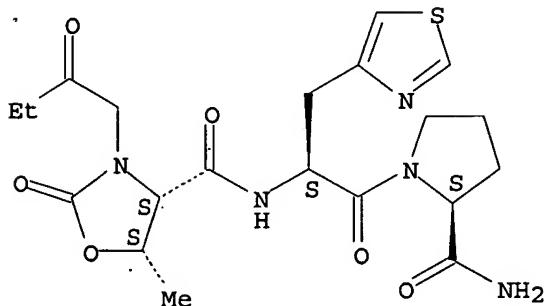
RN 204386-54-9 CAPLUS

CN L-Prolinamide, (4S,5S)-5-methyl-2-oxo-3-(2-oxobutyl)-4-oxazolidinecarbonyl-

10/229,819

3-(4-thiazolyl)-L-alanyl- (9CI) (CA INDEX NAME)

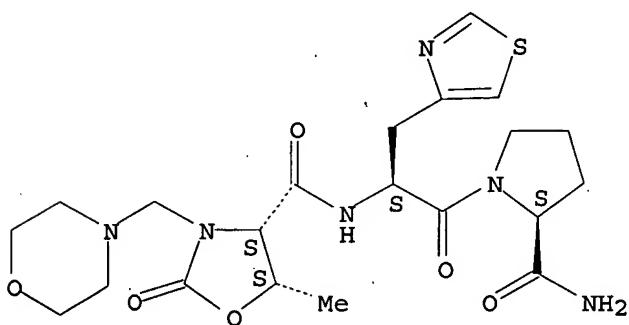
Absolute stereochemistry. Rotation (-).



RN 204386-58-3 CAPLUS

CN L-Prolinamide, (4S,5S)-5-methyl-3-(4-morpholinylmethyl)-2-oxo-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl- (9CI) (CA INDEX NAME)

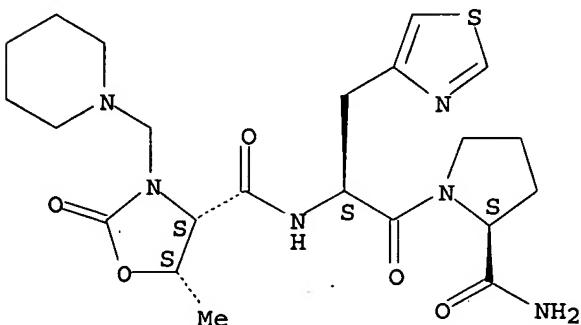
Absolute stereochemistry. Rotation (-).



RN 204386-60-7 CAPLUS

CN L-Prolinamide, (4S,5S)-5-methyl-2-oxo-3-(1-piperidinylmethyl)-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

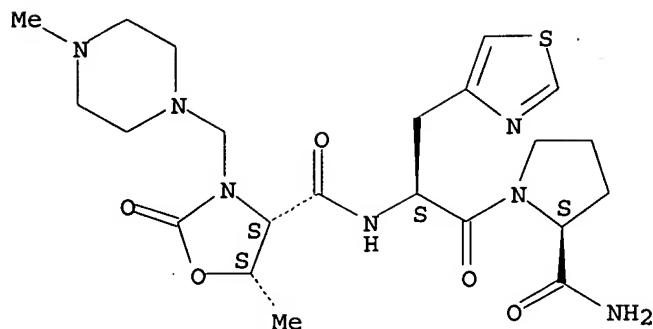


RN 204386-61-8 CAPLUS

CN L-Prolinamide, (4S,5S)-5-methyl-3-[(4-methyl-1-piperazinyl)methyl]-2-oxo-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

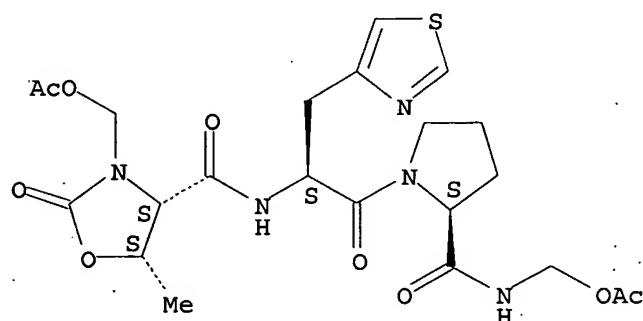
10/229,819



RN 204386-62-9 CAPLUS

CN L-Prolinamide, (4S,5S)-3-[(acetyloxy)methyl]-5-methyl-2-oxo-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl-N-[(acetyloxy)methyl]- (9CI) (CA INDEX NAME)

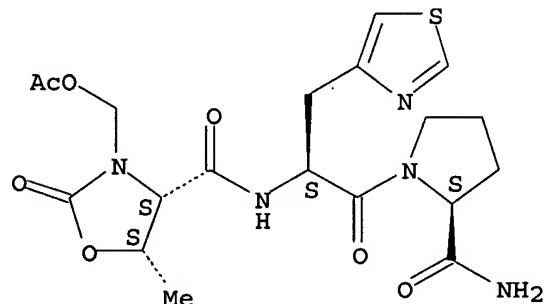
Absolute stereochemistry.



RN 204386-63-0 CAPLUS

CN L-Prolinamide, (4S,5S)-3-[(acetyloxy)methyl]-5-methyl-2-oxo-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl- (9CI) (CA INDEX NAME)

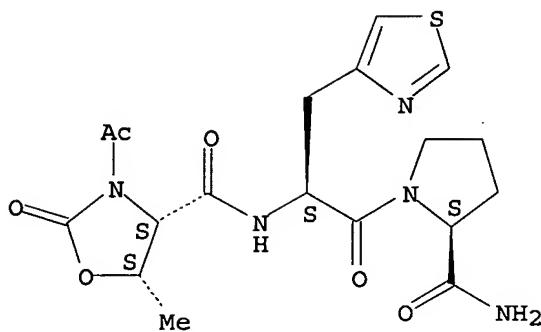
Absolute stereochemistry.



RN 204386-64-1 CAPLUS

CN L-Prolinamide, (4S,5S)-3-acetyl-5-methyl-2-oxo-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl- (9CI) (CA INDEX NAME)

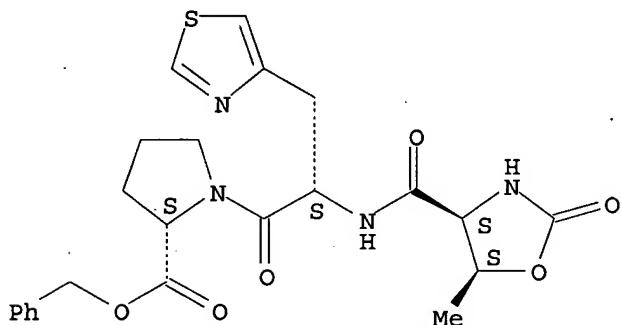
Absolute stereochemistry.



RN 204386-66-3 CAPLUS

CN L-Proline, (4S,5S)-5-methyl-2-oxo-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl-, phenylmethyl ester (9CI) (CA INDEX NAME)

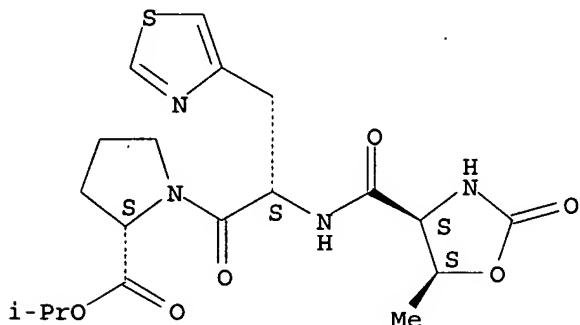
Absolute stereochemistry. Rotation (-).



RN 204386-67-4 CAPLUS

CN L-Proline, (4S,5S)-5-methyl-2-oxo-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl-, 1-methylethyl ester (9CI) (CA INDEX NAME)

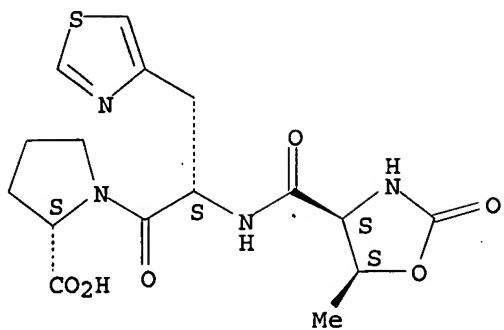
Absolute stereochemistry. Rotation (-).



RN 204386-68-5 CAPLUS

CN L-Proline, (4S,5S)-5-methyl-2-oxo-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl- (9CI) (CA INDEX NAME)

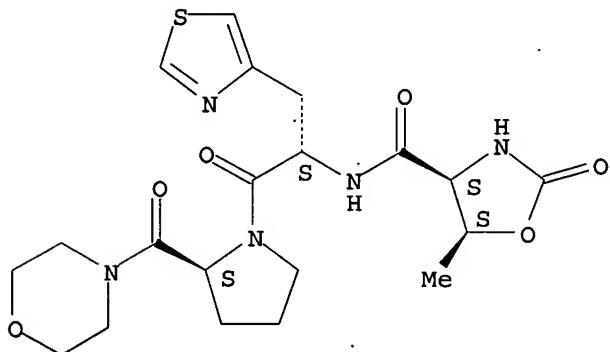
Absolute stereochemistry. Rotation (-).



RN 204386-70-9 CAPLUS

CN 4-Oxazolidinecarboxamide, 5-methyl-N-[2-[2-(4-morpholinylcarbonyl)-1-pyrrolidinyl]-2-oxo-1-(4-thiazolylmethyl)ethyl]-2-oxo-, [4S-[4α[R\*(R\*)],5α]]- (9CI) (CA INDEX NAME)

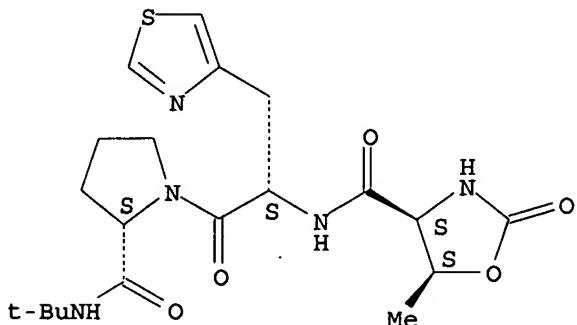
Absolute stereochemistry. Rotation (-).



RN 204386-71-0 CAPLUS

CN L-Prolinamide, (4S,5S)-5-methyl-2-oxo-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl-N-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

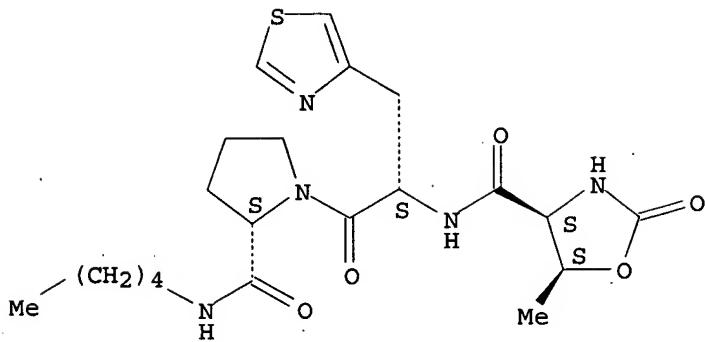


RN 204386-72-1 CAPLUS

CN L-Prolinamide, (4S,5S)-5-methyl-2-oxo-4-oxazolidinecarbonyl-3-(4-thiazolyl)-L-alanyl-N-pentyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

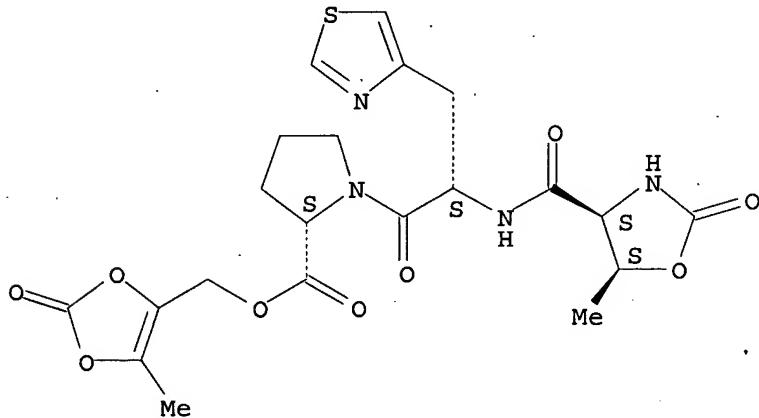
10/229,819



RN 204386-73-2 CAPLUS

CN L-Proline, (4S,5S)-5-methyl-2-oxo-4-oxazolidinecarboxyl-3-(4-thiazolyl)-L-alanyl-, (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl ester (9CI) (CA INDEX NAME)

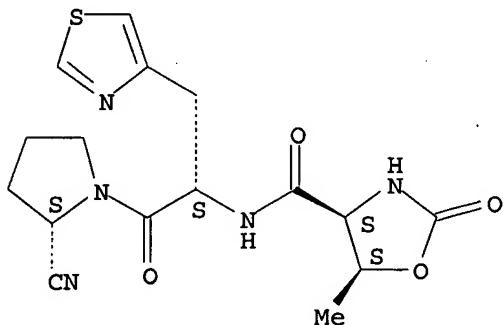
Absolute stereochemistry. Rotation (-).



RN 204386-74-3 CAPLUS

CN 4-Oxazolidinecarboxamide, N-[(1S)-2-[(2S)-2-cyano-1-pyrrolidinyl]-2-oxo-1-(4-thiazolylmethyl)ethyl]-5-methyl-2-oxo-, (4S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

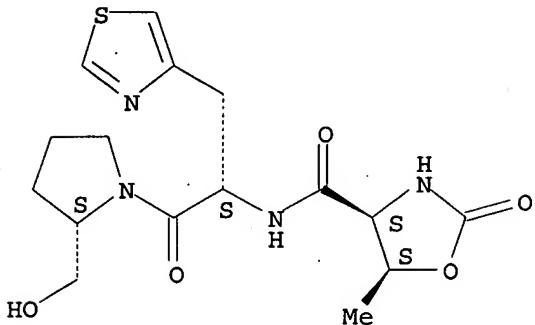


RN 204386-75-4 CAPLUS

CN 4-Oxazolidinecarboxamide, N-[2-[(2S)-2-(hydroxymethyl)-1-pyrrolidinyl]-2-oxo-1-(4-thiazolylmethyl)ethyl]-5-methyl-2-oxo-, [4S-[4a[R\*(R\*)],5a]]- (9CI) (CA INDEX NAME)

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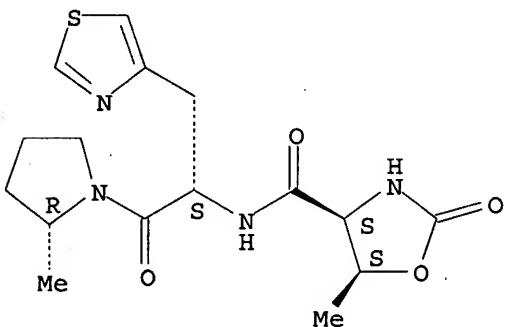
Absolute stereochemistry. Rotation (-).



RN 204386-76-5 CAPLUS

CN 4-Oxazolidinecarboxamide, 5-methyl-N-[(1S)-2-[(2R)-2-methyl-1-pyrrolidinyl]-2-oxo-1-(4-thiazolylmethyl)ethyl]-2-oxo-, (4S,5S)- (9CI)  
(CA INDEX NAME)

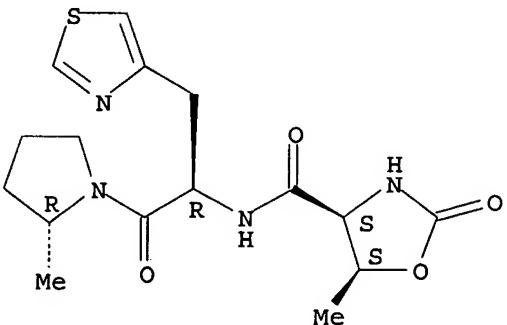
Absolute stereochemistry. Rotation (-).



RN 204386-77-6 CAPLUS

CN 4-Oxazolidinecarboxamide, 5-methyl-N-[2-(2-methyl-1-pyrrolidinyl)-2-oxo-1-(4-thiazolylmethyl)ethyl]-2-oxo-, [4S-[4a[S\*(S\*)],5a]]- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



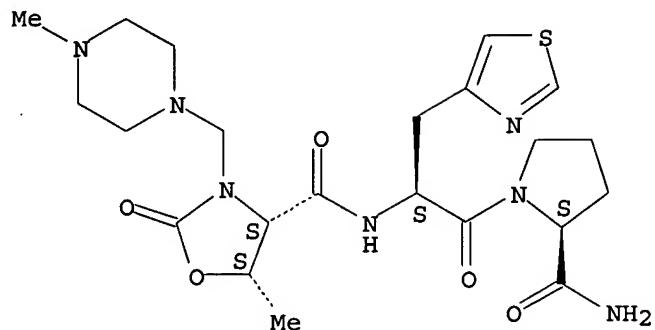
RN 204506-84-3 CAPLUS

CN L-Prolinamide, (4S,5S)-5-methyl-3-[(4-methyl-1-piperazinyl)methyl]-2-oxo-4-oxazolidinecarboxyl-3-(4-thiazolyl)-L-alanyl-, hydrochloride (5:9) (9CI)

10/229,819

(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



● 9/5 HCl

REFERENCE COUNT:

14

THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT